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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,513	12/13/2005	Nathalie Marie-Josephe Garcon	VB60298	6380

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

NOTIFICATION DATE	DELIVERY MODE
11/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/560,513	GARCON ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-16, 18-35, 37, 39, 41-48, 51 and 53-61* is/are pending in the application.

4a) Of the above claim(s) *35,37,39,41-48,51 and 53-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-16,18-34,60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment submitted on 7/29/08 is made. Claims 12-16, 18-34, 60 and 61, and the Species DTPw (diphtheria toxoid, tetanus toxoid and inactivated whole-cell B.pertussis) and DTPa (diphtheria toxoid, tetanus toxoid and inactivated acellular B.pertussis) are currently under examination.

Claims 35, 37, 39, 41-48, 51, and 53-59 were previously withdrawn from consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112-2nd paragraph

1. Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of claim 61 cannot be understood because it is unclear which adjuvants possess a 'zero point charge greater than 8' and can 'reduce the immunological interference that the adjuvant has on PRP. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The structure of these adjuvants is not readily apparent. Clarification and correction is requested.

Claim Rejections - 35 USC § 112-Scope of Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 12, 14-16, 18-34, 60 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising a PRP of H.influenzae B and a polyanionic homopolymer which is poly-L-glutamic acid (PLG) and aluminum hydroxide adjuvant, wherein PLG reduces the immunological interference that the adjuvant has on PRP, does not reasonably provide enablement for an immunogenic composition comprising a PRP of H.influenzae B and ***any*** polyanionic homopolymer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification teaches that Applicants have discovered that adding PLG to a vaccine comprising PRP and aluminum hydroxide allows for the PLG to compete with PRP thereby protecting it from any aluminum hydroxide present in the vaccine, e.g., by reducing the amount or rate of binding of PRP to adjuvant and/or the extent or rate of floccuation, yet surprisingly does not cause antigens already absorbed to aluminum hydroxide to become significantly desorbed. However, the results in the instant specification do not demonstrate the use of any other polyanionic polymer which can achieve these results. The instant specification broadly claims an immunogenic composition comprising a PRP of H.influenzae B and ***any*** polyanionic homopolymer

which represents an extremely large class of compounds. The specification provides a very large and broad description of what constitutes the invention's 'polyanionic homopolymer' see pages 6-7 of the instant specification. However, the working examples and results have only shown results using PLG (poly-glutamic acid) as the polyanionic homopolymer. The specification teaches that the prior art has taught the use of PLG (poly-glutamic acid) as a drug delivery for caner therapy and as a biological glue and that the inventors now show its use as an excipient for intramuscular vaccination. It is noted that the instant claims do not require the polyanionic polymer to have all negatively charged repeat units, but states that the polymer should prevent flocculation between PRP and aluminum hydroxide adjuvant and/or the capability not to significantly desorb antigens beneficially adsorbed to aluminum hydroxide. It would take undue experimentation for one of skill in the art to discover another polyanionic homopolymer from the very large description of the homopolymers which would work in this capacity. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the

specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Payne-LG et al (Dev. Biol. Stand. 1998. 92: 79-87. "PCPP as a parenteral adjuvant for diverse antigens').

Payne et al analyze the adjuvanticity of the phophazene polymer (polyanionic polymer), poly[di(carboxylatophenoxy) phospazene (PCPP) with a diverse collection of immunogens. PCPP is shown to be a potent adjuvant for capsular polysaccharides PRP from H.influenzae type b. PCPP is a superior adjuvant at least with TT compared to similar negatively charged polyanions, polymethylacrylic and polyacrylic acid (abstract; p. 84-86).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 14-16, 18-34, 60 and 61are rejected under 35 U.S.C. 103(a) as being unpatentable over Payne-LG et al (Dev. Biol. Stand. 1998. 92: 79-87. “PCPP as a parenteral adjuvant for diverse antigens') in view of Boutriau et al (WO 02/00249)and Database Medsafe NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY; 2002, GLAXOSMiTHKLINE NZ LTD: "Datasheet . Hiberix" XP002306401 retrieved from H1-1"P:/ANWW.MEDSAFE.GOV-r.NZJPROFS/DATASHEET/H/HIBERIXINJ, HTM..

Payne et al analyze the adjuvanticity of the phophazene polymer (polyanionic polymer), poly[di(carboxylatophenoxy) phospazene (PCPP) with a diverse collection of immunogens. PCPP is shown to be a potent adjuvant for capsular polysaccharides PRP from H.influenzae type b. PCPP is a superior adjuvant at least with TT compared to similar negatively charged polyanions, polymethylacrylic and polyacrylic acid (abstract; p. 84-86).

However, Payne does not specifically teach the incorporation of one or more further antigens into the composition comprising the antigens specifically disclosed in instant claims 20-22, 25, 31-32 and 60.

Boutriau et al teach a multivalent immunogenic composition comprising a conjugate of a carrier protein (tetanus toxoid, diphtheria toxoid, CRM197, protein D...) and the capsular polysaocharide of H. influenza type B, wherein said composition additionally comprise 2 or more further bacterial polysaccharides (e.g.N. meningitidis Y or W polysaccharide, Streptococcus pneumoniae 1…). One specific DTPw composition disclosed comprises: "TT, DT; Pw HepB (perferably adsorbed onto Al-phosphate), Hib

(preferably conjugated onto "TT and/or unadsorbed), MenA (pref, conjugated onto protein-D) and MenO (pref conjugated onto protein D). Combination vaccines accordlng to Boutriau require substantially lower doses of Hib to obtain at least equivalent Ab titers. Boutriau mentions, that due to the known effect of carrier suppression, it is advantageous if in each of the compositions of the invention the polysaccharide Ag contained therein are conjugated to more than one carrier (p 3, lines 2-7, 23-33; p 5, 1ines 18-21; claims 12-15, 19, 20, 27-29).

Database Medsafe teaches that Hiberix (unabsorbed Hib-TT) can be mixed in the same syringe with SmithKline Beecham vaccine Infanrix (DTPa vaccine), Tritanrix (DTPw vaccine) or Tritanrix-HB (DTPw-HB vaccine).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent evidence to the contrary, that one or more further antigens could be added into the compositions taught by Payne, specifically the antigens recited in instant claims 20-22, 25, and 31-32 because Boutriau and Database Medsafe specifically teach these type of combination vaccines with success. Boutriau specifically teaches one DTPw composition disclosed comprises: "TT, DT; Pw HepB (perferably adsorbed onto Al-phosphate), e.g., instant claims 31 and 32. Although the Payne do not explicitly recite the concentrations of polyanionic polymers and amount of the Hib oligosaccharide/polysaccharide as recited in instant claims 14-18, these are result effective variables. The specific amount of adjuvant in the range of 100-1000 micrograms per 0.5mL dose as recited in instant claim 28 is a little bit higher than that disclosed in the primary references; however, it is in the same range. It has long been

settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 14-16 and 18 are for any particular purpose or solve any stated problem and the prior art teaches that the concentration of the active ingredients and carriers of vaccines/immunogenic compositions often vary according to the subject being treated and the antigen which is being used, solutions and parameters appear to work equally as well, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the ingredients taught in the Payne reference by normal optimization procedures known in the bacterial immunological arts.

8. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Payne-LG et al (Dev. Biol. Stand. 1998. 92: 79-87. “PCPP as a parenteral adjuvant for diverse antigens') in view of Sanchez et al (Internat. J. Pharmaceutics. A99. 185: 255-266. ‘Poly (lactide-co-glycolide) microspheres’), Watson et al (Vet. Microbiol. 34: 139-153. 1993) and Hilgers (WO 98/17310).

Payne et al analyze the adjuvanticity of the phophazene polymer (polyanionic polymer), poly[di(carboxylatophenoxy) phospazene (PCPP) with a diverse collection of immunogens. PCPP is shown to be a potent adjuvant for capsular polysaccharides PRP from H.influenzae type b. PCPP is a superior adjuvant at least with TT compared to similar negatively charged polyanions, polymethylacrylic and polyacrylic aci

However, Payne does not teach the polyanionic polymer to be poly-L-glutamic acid (PLG).

Sanchez, Watson and Hilgers teach that a variety of different polyanionic polymers can be used in order to prepare alternative immunogenic formulations. Sanchez specifically teaches the use of PLG microspheres. See abstract.
Hilgers et al teach the use of a large variety of different polyanionic polymers as adjuvants for mucosal immunization with bacterial and/or viral antigens. See pages 4-8 of Hilgers et al which specifically teaches the same polyanionic polymers as recited in the instant specification. Watson teaches a variety of different adjuvants, including polyanionic polymers.

It would have been prima facie obvious at the time the invention was made that the polyanionic polymer taught by Payne et al could be substituted with a variety of different polyanionic polymers, including PLG as specifically taught by Sanchez, because they would expect to act as functional equivalents, absent evidence to the contrary.

Response to applicants' arguments:

9. Applicants' arguments are rendered moot due to the new grounds of rejection.

10. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

11/5/08